HEALTHCARE • EDITORS' PICK

The WHO To Discuss Global Pandemic Treaty At World Health Assembly May 22-28

Bruce Y. Lee Senior Contributor
I am a writer, journalist, professor, systems modeler, computational and digital health expert, avocado-eater, and entrepreneur, not always in that order.
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May 18, 2022, 12:54pm EDT

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The World Health Organization (WHO) will be discussing a possible Global Pandemic Treaty at the ...
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You know the 1996 movie *Independence Day*, where much of the World united to defeat a common enemy? Well, during the Covid-19 pandemic that started in 2020, pretty much the opposite happened. The World was about as organized as all-cat produced and directed episode of *Dancing with the Stars or* rather *Dancing with the Stars Who are Also Cats*. The global pandemic response had relatively little coordination, little unity. In fact, it was more like the 1983 and 2009 TV miniseries *V*, where many politicians, personalities, social media accounts and others seemed like they were actually trying to help the enemy, in this case, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). That allowed the virus to kill over 6.27 million people and counting, leave potentially millions upon millions more with long Covid, and cost society boatloads of money. That's why the World Health Organization (WHO) will be discussing a possible Global Pandemic Treaty at the upcoming 75th World Health Assembly in Geneva, Switzerland, from May 22 to 28. Yet, despite the clear need for more global coordination, some politicians, some celebrities, and a bunch of social media accounts have been trying to, guess what, argue against such a treaty. They even started a hashtag #StopTheTreaty.

Yeah, having no global agreement in place before the next pandemic is going to work out real well, right? Picture a football team running on to the field for a championship game with no real plan, no real strategy, no real agreement to play together, and players saying, "I will do whatever I want with the ball, because you know, freedom." Things don't go well when people do whatever they want with their balls, meaning the kind that you kick and throw, during a team sporting event. Similarly, having each country or even each faction within each country do whatever they want is going to end up in disaster. This is essentially what's ended up happening in the U.S., which has suffered over a million dead since the start of the pandemic.

In a commentary published in *The Lancet* on May 16, a team of authors, most of whom are from the U.K., wrote that "the Covid-19 pandemic has highlighted profound weaknesses in the global governance of health; inadequate preparation, coordination, and accountability hampered the collective response of nations at each stage." They asserted that "Changes to the global health architecture are necessary to mitigate the health and socioeconomic damage of the ongoing pandemic, and to prepare for the next major global threat to health." They indicated that "success will require clear demarcations of responsibility with a parsimonious role for international institutions. Although a pandemic treaty or alternative new instrument or process cannot solve all that is wrong with global health, it can deliver targeted improvements if supported by effective and clear global governance."

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Some have claimed that the Covid-19 pandemic is a once-in-a-lifetime or once-in-a-century event. Having a pierogi fall right into your mouth after a chain of events triggered by your cat may be a once-in-a-lifetime event. But the same probably won't be true for pandemics. Chances are the World will see yet another infectious pandemic in the near future, if not multiple pandemics. In fact, anyone who was born before the *Twilight* movie saga began has already experienced two pandemics: the 2009 H1N1 flu pandemic and the current Covid-19 one. Keep in mind what's happened since the severe acute respiratory syndrome (SARS) of 2003 left over 8,000 sick and at least 774 people dead. In the less than two decades that have followed, a new infectious disease threat has emerged seemingly every two or so years, ranging from the Middle East Respiratory Syndrome (MERS) to the Zika virus. In fact, with climate change displacing plant and animal life around the world, the likelihood of more viruses and other pathogens jumping from other animal species to humans may increase, along with the risk of another pandemic occurring.

As the Covid-19 pandemic has demonstrated, viruses and other pathogens do not respect geopolitical borders. They don't have to carry little EZ Passes or passports with their spikes. Therefore, as long as a pathogen is spreading fairly widely in one location, it remains a threat for everyone around the world.

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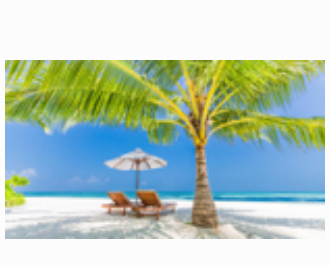
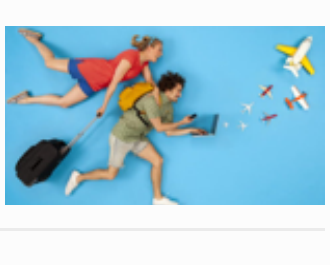
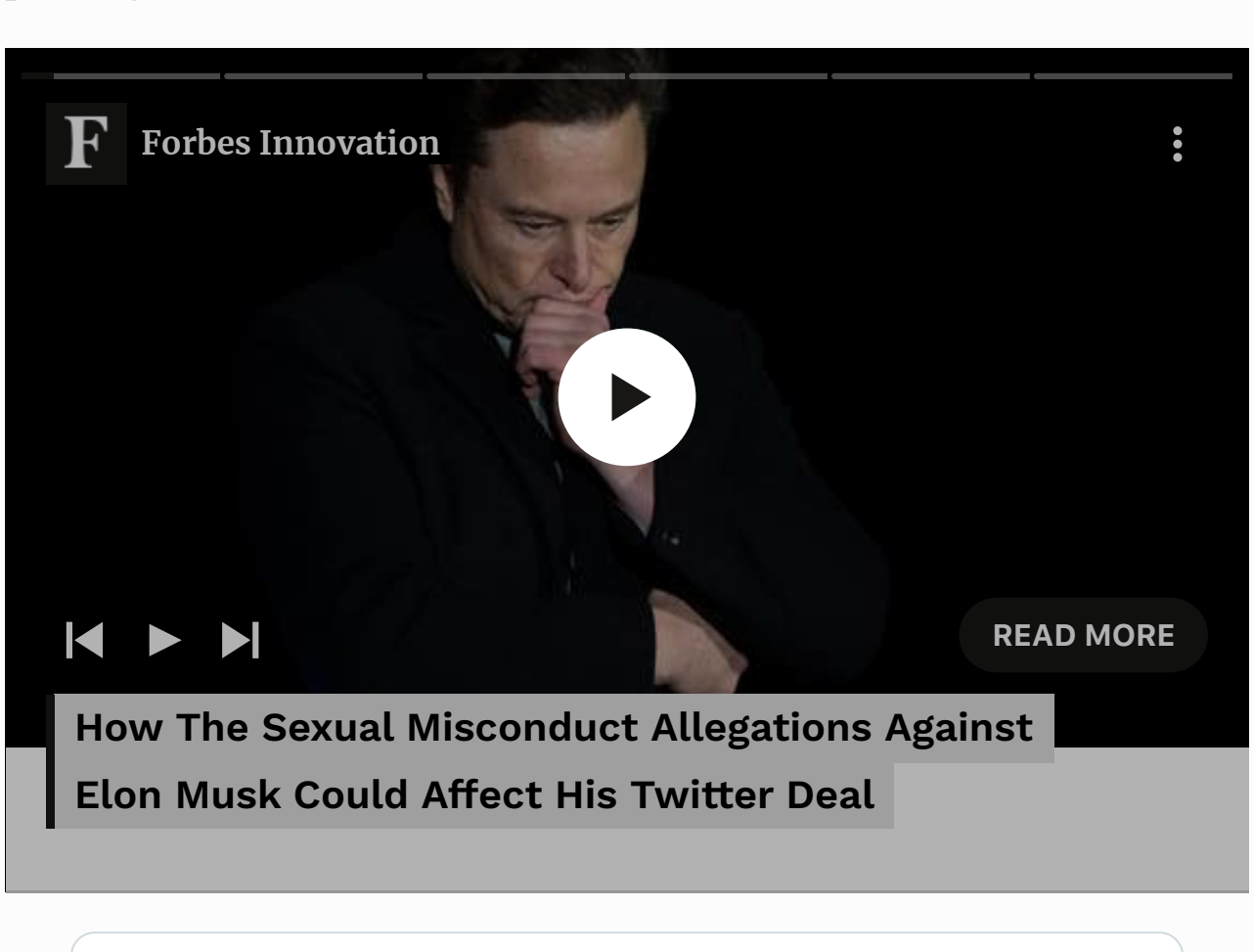




Imagine how much suffering could have been avoided and how many lives could have been saved if only countries around the world had been more unified and coordinated with each other to combat the Covid-19 coronavirus. What if countries had warned each other earlier about the original SARS-CoV-2 and the emergence of new variants? What if countries had coordinated more on supporting and sharing research? What if they had more effectively pooled together knowledge and resources to further accelerate the development and implementation of new technologies and approaches for virus surveillance, prevention, and treatment? What if governments had banded together to negotiate better terms with vaccine, drug, and test manufacturers? What if countries had worked together to combat misinformation and support science?

Who wouldn't have wanted better global coordination since early 2020? Well, apparently not the WHO and anyone who would've wanted the SARS-CoV-2 to have been better controlled, which should be everyone that isn't shaped like a spiky massage ball. Yet, the WHO was trending on Tuesday with a number of social media accounts using the hashtag #StopTheTreaty. For example, James Melville, whose Twitter profile describes himself as a freelance writer, pundit, and liberal, tweeted out a video with actor Russell Brand that included some very naughty words (WARNING: don't look at the following tweet if you're sensitive to expletives that rhyme with feather-plucking):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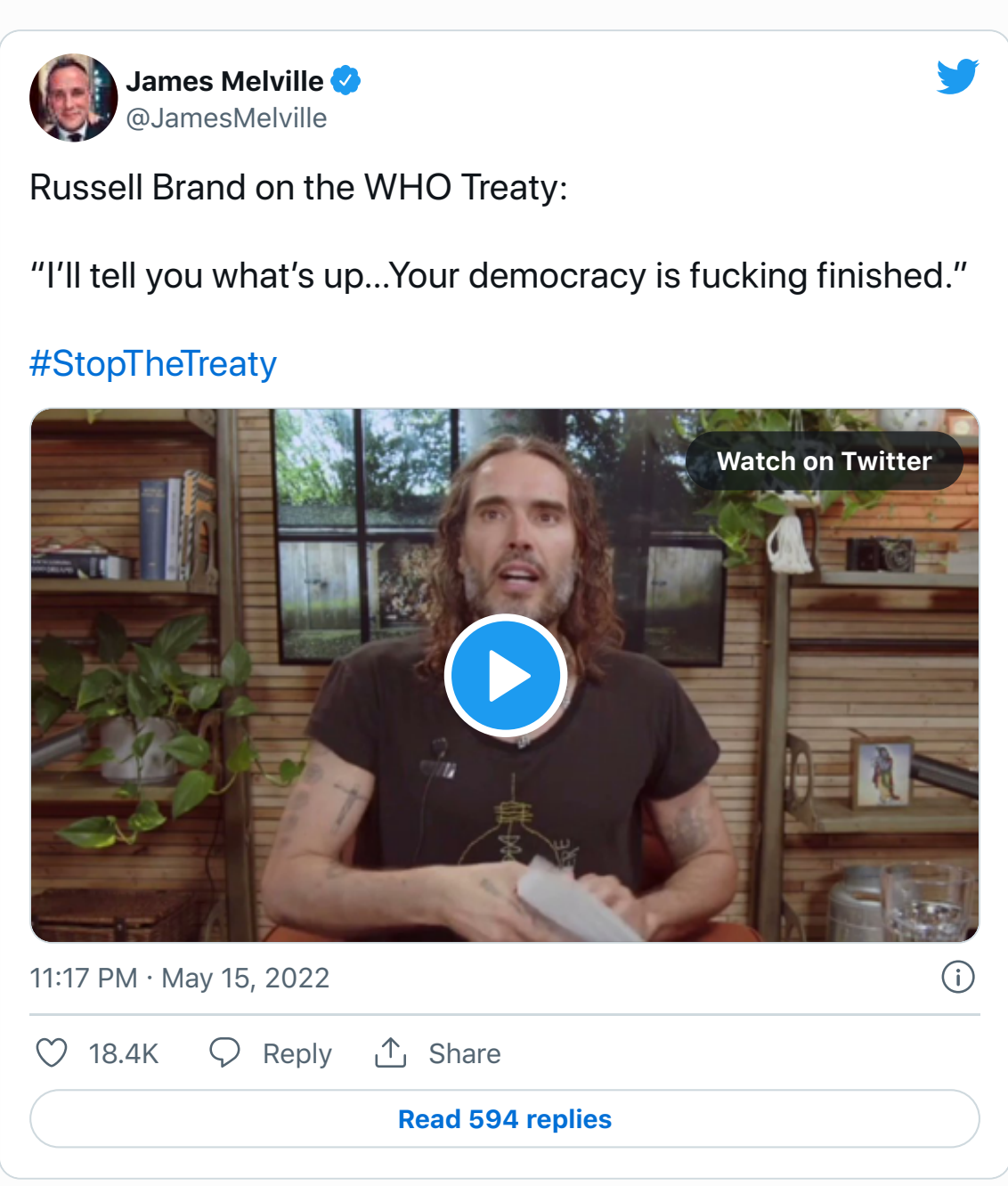

James Melville
@JamesMelville

Russell Brand on the WHO Treaty:

"I'll tell you what's up...Your democracy is fucking finished."

#StopTheTreaty

11:17 PM · May 15, 2022

18.4K Reply Share

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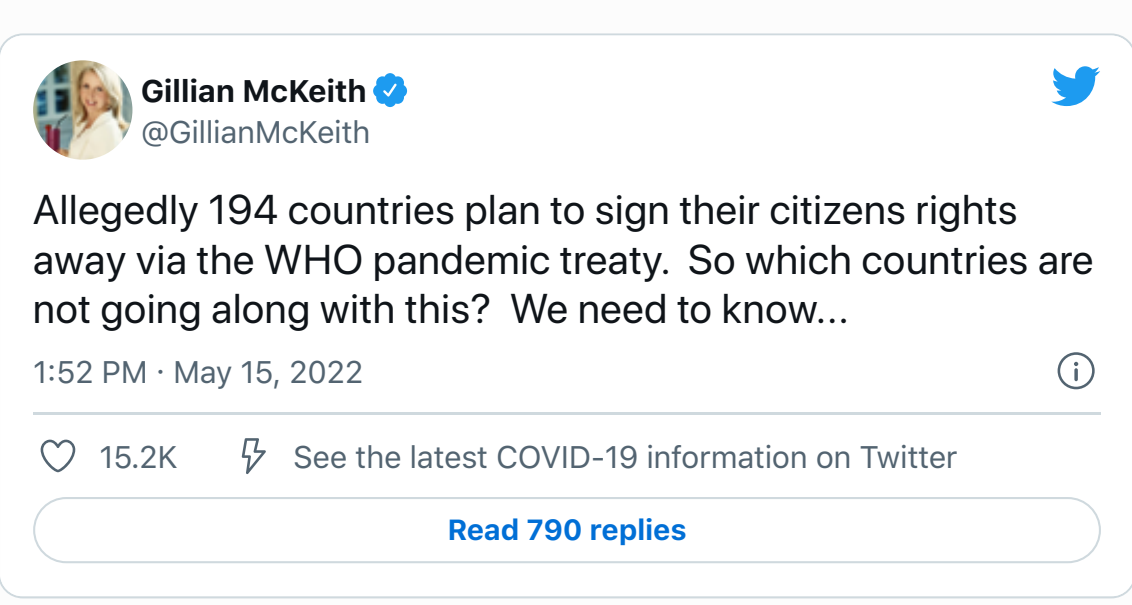
Yeah, when you think science and global health, the first name that comes to your mind is Russell Brand, right? In the video, Brand claimed that a global pandemic treaty will be a "boot on your face forever" and that "the WHO will be in charge" of presumably the world. Umm, first of all, the WHO doesn't have feet and thus doesn't wear boots. Secondly, the WHO's so-called power is completely dependent on what the 194 member states (otherwise known as countries around the world) want and the resources that are allocated to the WHO. And anyone who has ever seen the WHO offices should realize that the organization isn't exactly swimming in money. The budget originally allocated for WHO for 2020-2021 was $5. 84 billion, which was just a little more than the $5.5 billion that Jeff Bezos spent to be in space for about four minutes, according to Joe McCarthy writing for *Global Citizen*. The WHO also clearly lists the sources of their funding.

Brand went on to claim that once a global pandemic treaty, people will look back at it and say: "we lapsed into a terrible technocratic globalist agenda where ordinary people have no ability to influence democratic outcomes where the media cooperated in keeping people distracted, numb, and dumb while the powerful funded non-democratic organizations to carry out their edicts." Well, that's some interesting Brand management of the situation. Brand said all that without even seeing what such a treaty would look like. Isn't that a bit like saying that you don't believe in any contracts or any treaties anywhere? What if a studio were to tell Brand, "we'd like you to act in this movie but don't believe in issuing contracts?"

Then there were tweets from some folks like Gillian McKeith, who describes herself as a "television presenter. nutritionist & dietetic technician. No.1 bestselling author" and "the 'Poo' Lady" on her Twitter profile. She claimed that "194 countries plan to sign their citizens rights away via the WHO pandemic treaty" *before* anyone knows what specifically such a treaty may stipulate:



Gillian McKeith
@GillianMcKeith

Allegedly 194 countries plan to sign their citizens rights away via the WHO pandemic treaty. So which countries are not going along with this? We need to know...

1:52 PM · May 15, 2022

15.2K See the latest COVID-19 information on Twitter

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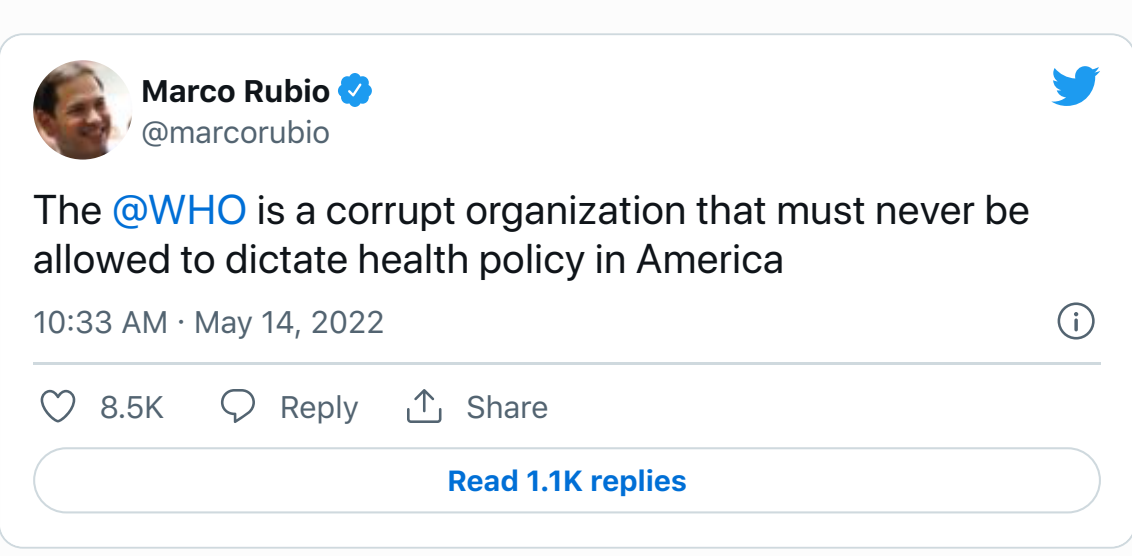
Meanwhile, Senator Marco Rubio (R-Florida) asserted that "the WHO is a corrupt organization that must never be allowed to dictate health policy in America" in the following tweet:



Marco Rubio
@marcorubio

The @WHO is a corrupt organization that must never be allowed to dictate health policy in America

10:33 AM · May 14, 2022

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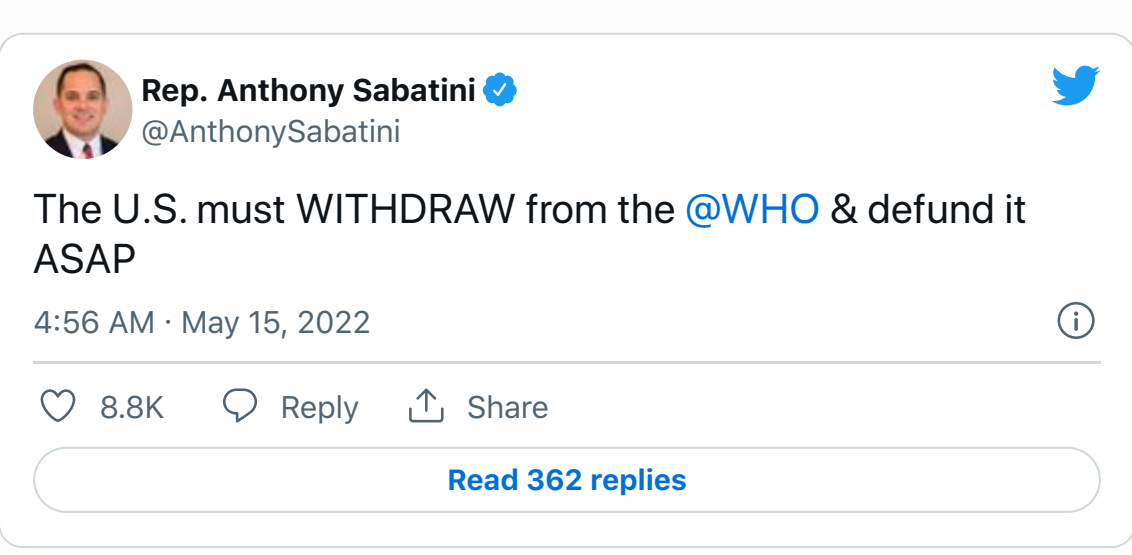
While the WHO certainly has had its issues that need to be addressed, is blanketly calling the WHO corrupt without pointing to specifics that fair? Wouldn't that be like saying that "politicians are corrupt and should never be allowed to dictate policy in America?" Plus, the U.S. should have a say in what the WHO does, assuming that the U.S. continues to serve as the WHO's biggest donor and participate in the WHO. U.S. Secretary of State Antony J. Blinken, JD, and Secretary of Health and Human Services Xavier Becerra, JD, did call for a strengthening of global health security in a August 31, 2021, commentary for *JAMA*. They argued that "global leaders must modernize essential global institutions, starting with the World Health Organization (WHO)."

Gee, what would actually remove the U.S. from the WHO decision making process? How about "withdrawing from the WHO" as Florida House of Representatives member Anthony Sabatini (R) demanded:



Rep. Anthony Sabatini
@AnthonySabatini

The U.S. must WITHDRAW from the @WHO & defund it ASAP

4:56 AM · May 15, 2022

8.8K Reply Share

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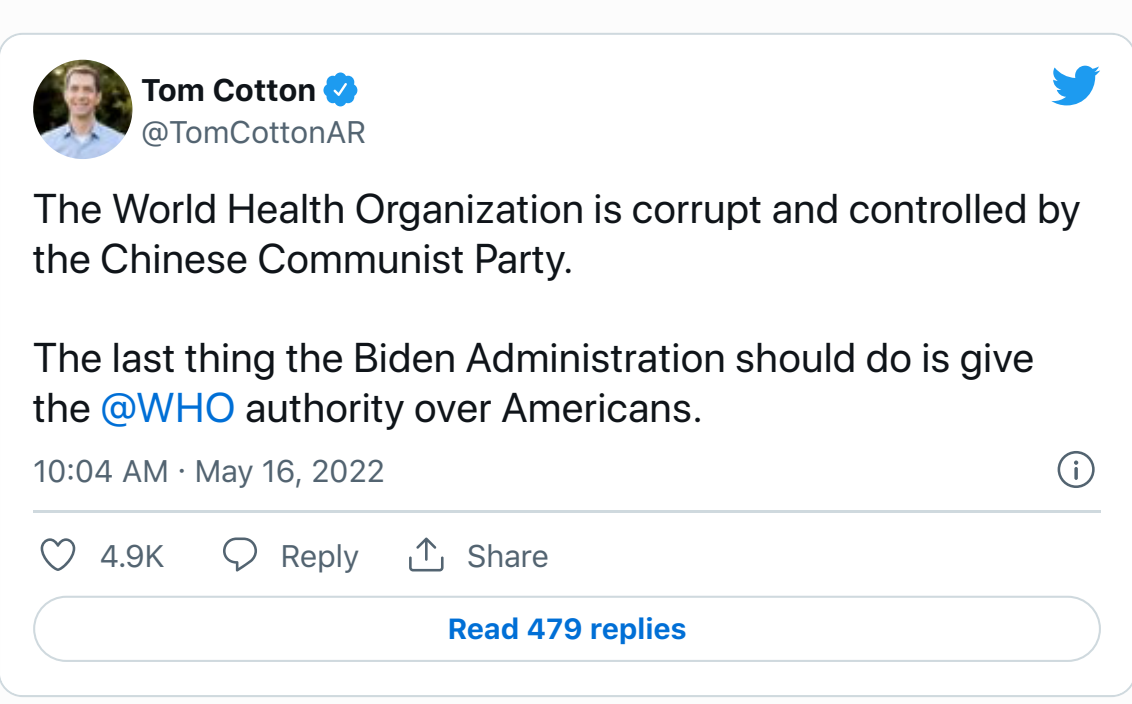
Umm, didn't then-U.S. President and current Mar-A-Lago resident Donald Trump try to do such a thing back in 2020? How did that end up working out? Isolating oneself from global decision making hasn't tended to work out well for countries in the past. For example, years of isolationism ended up weakening China, leaving them susceptible to invasion by Japan prior to World War II and eventual take over by the Communist Party after World War II.

Speaking of China, here's what Rep. Tom Cotton (R-Arkansas) tweeted:



Tom Cotton
@TomCottonAR

The World Health Organization is corrupt and controlled by the Chinese Communist Party.

The last thing the Biden Administration should do is give the @WHO authority over Americans.

10:04 AM · May 16, 2022

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What exactly is the evidence that the WHO is controlled by the Chinese Communist Party? In fact, a stronger WHO might be able to push China into being more open and more transparently sharing information about any possible infectious disease threats and outbreaks. An important question is whether the Covid-19 pandemic could have been better mitigated had China had better disease surveillance systems, alerted the rest of world earlier about the initial SARS-CoV-2 cases, and collaborated more globally on early containment strategies.

Another China-related issue is why the WHO continues to exclude Taiwan from its membership. The world has much to learn from Taiwan's effective SARS-CoV-2 containment strategies and other public health measures. Therefore, if you are worried about China's influence, wouldn't it make sense to push for more involvement of other East Asian governments such as Taiwan's?

Ultimately, those opposing any global pandemic treaty don't seem to be offering any viable alternatives to improve the world's ability to prevent and control pandemics. It's easy to criticize anything and keep yelling words such as "freedom" kind of how babies fight against wearing clothes and insist on pooping whenever they want to do or doo-doo so. What's much more difficult is finding solutions.

If invaders from outer space were to appear now as they did in *Independence Day*, our world would be kind of in trouble. You'd have politicians, TV personalities, and others claiming that the invaders aren't real and even siding with them. Our world needs to be more unified in order to more effectively fend off any major threats to our health, whether its infectious disease, non-communicable disease like obesity, or aliens with tentacles and telepathic ability. Remember what that John McClane character said in the 1988 movie *Die Hard*: "Now, you listen to me, jerk-off. If you're not part of the solution, you're part of the problem. Quit being part of the [bleeping] problem and put the other guy back on!" It's time to put real science and health experts back on.

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Bruce Y. Lee Follow

I am a writer, journalist, professor, systems modeler, computational and digital health expert, medical doctor, avocado-eater, and entrepreneur, not always in that... **Read More**

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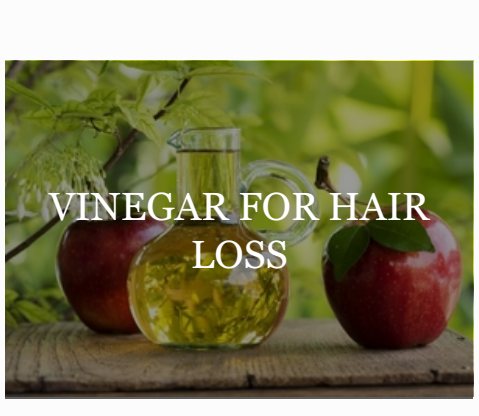

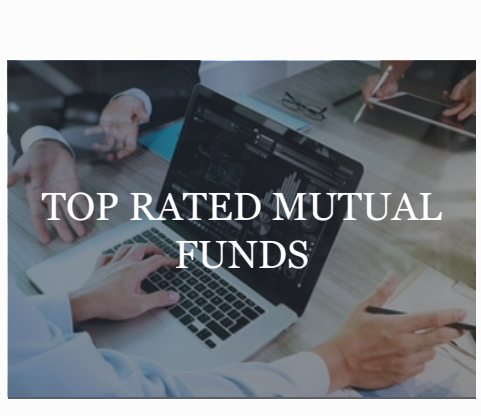

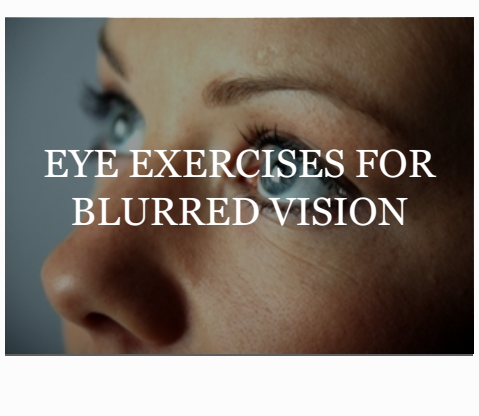
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INNOVATION

How Consumer Demand Is Driving Innovation For Mobility Service Providers

Google Maps Platform Contributor Brand Contributor
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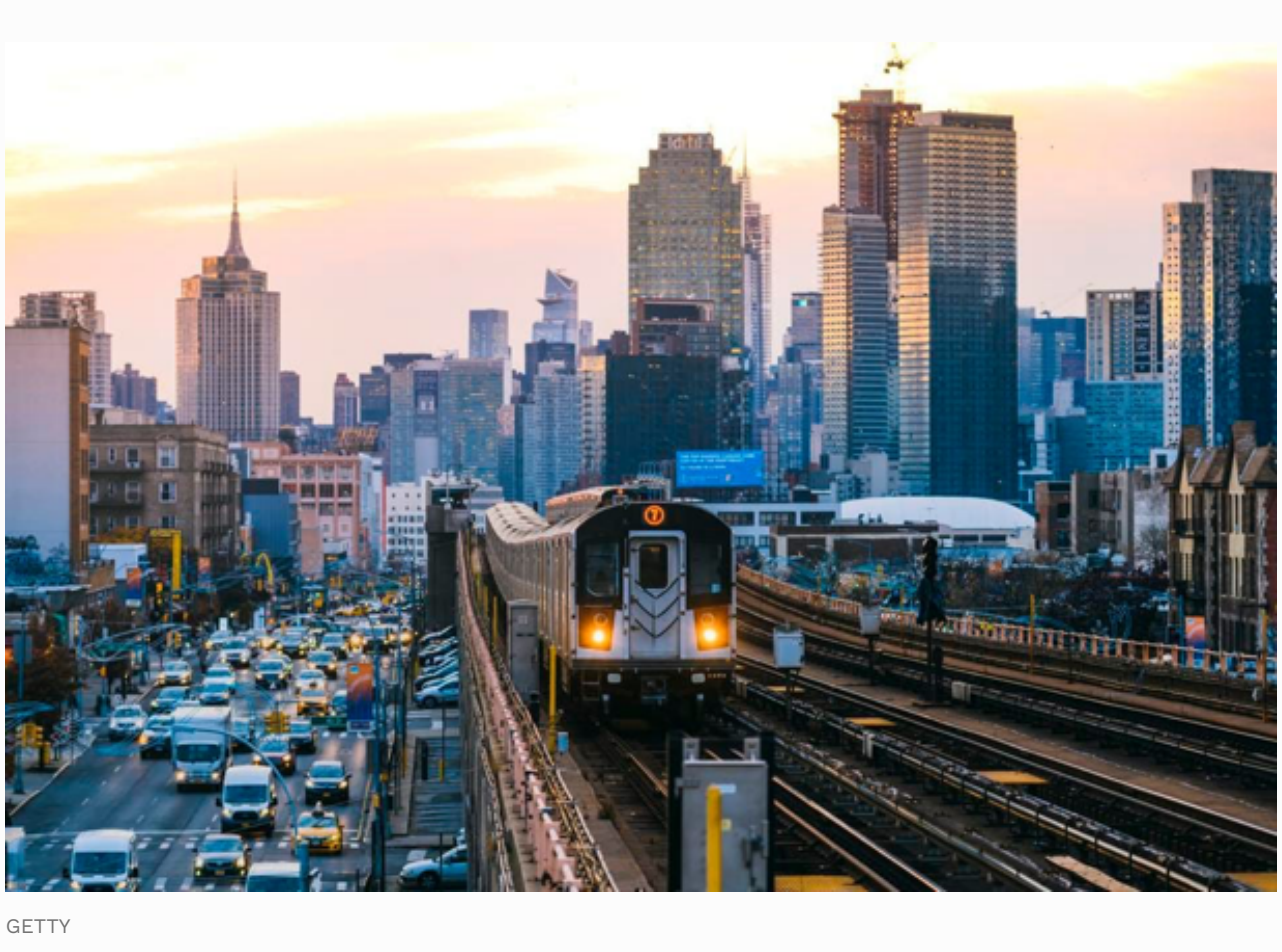
Mar 24, 2022, 12:35pm EDT

Running a modern vehicle fleet is more than just delivery trucks, cardboard boxes and pre-scheduled routes. In addition to serving a more diverse set of delivery use cases driven by e-commerce, huge fleets have grown to support consumers' use of on-demand ride services.

Moving packages and moving riders both fall under the term "mobility services," and both depend on keeping drivers productive and seamlessly orchestrating multiple parties in the real world.



GETTY

To make all this possible, mobility operators look to geospatial data and capabilities from providers such as Google Maps Platform.

"You cannot stand up a mobility service, whether you're moving riders or goods, without really strong maps, routing and geospatial data," says Shalin Mantri, group product manager at Google Maps Platform.

For example, in the wake of the pandemic, consumers continue to expect more from e-commerce. They want their packages to arrive where and when they want, and at the lowest cost possible—or, ideally, for free. This has put further strain on already-stressed supply chains.

"The supply chain space is an incredibly complex ecosystem with many interacting parts," says Nick DeMeuse, product manager at Google Maps Platform. "Getting the last mile right is of the utmost importance to prevent that complexity from negatively impacting consumers' delivery experience."

In other words, if you can create a great delivery or pickup experience even during a supply chain crunch, it will go a long way to keeping your customers happy.

But how?

The Road To Rapid Delivery

For much of modern American life, the acceptable window in which to deliver a package was several days long, maybe even weeks. That's because home delivery was the unusual use case. Most purchases were made in physical stores, and customers drove to their favorite shops in their own cars.

That changed with the arrival of digital mapping and navigation. As more of the world's highways and byways—and, crucially, local streets—were digitized, delivery routes and schedules became more efficient. On-demand delivery and ride-share capabilities increased—as did customer expectations.

But it wasn't the big names in delivery who were leading the charge. Largely, it was digital-native developers finding new and novel uses for this mapping data.

"The launch of app stores and developer software developer kits lit a wildfire of innovation. Overnight, developers had the ability to build experiences that bridged the digital and physical worlds. App-based ride-sharing, for instance, became a reality thanks to democratized access to digital maps and geospatial data," says Mantri.

Although same-day deliveries became more common during the pandemic, Mantri believes tighter windows were inevitable.

"Covid-19 accelerated that trend," he says. "But I don't think it's Covid-19 itself that shifted consumer behavior. It's a decades-long trend, if not longer, where consumers want more convenience. We want things faster. We want things at lower cost."

Looking beyond Covid-19, mobility services must make plans *now* to keep pace with current consumer demands while also preparing for the demands of tomorrow.

Google Maps Platform—with frequently updated geospatial data that covers more than 250 countries and territories—aims to accommodate the rapid growth and dynamic experiences that providers are bringing to market.

Improving On-Demand Rides And Deliveries

At a large, established delivery company, it's not uncommon for the same driver to service the same route for years. That driver knows who's not home during the day, whose doorbells don't work and which neighbors will sign for packages. This familiarity brings efficiency in the form of fewer missed deliveries.

But this institutional knowledge is not shareable at scale. The new generation of on-demand delivery services—and ride-hailing apps that offer local food and package delivery—have had to attract new drivers to their platforms while maintaining high service quality and productivity.

To meet these needs, in 2020, Google Maps Platform introduced the On-Demand Rides & Deliveries solution, a suite of capabilities like turn-by-turn navigation integrated into drivers' apps, and trip and order progress with real-time visibility for consumers. The solution has been adopted by leading ride-hailing and on-demand delivery operators, helping all drivers, whether they're full-time delivery personnel, seasonal employees or part-time gig workers, function more efficiently.

"We've provided a set of tools that our customers can use to build out what they think are the best experiences for their diverse sets of drivers," DeMeuse says. "They have better predictability around what things are going to look like for their day."

To put it another way, Mantri says, "You can almost give superpowers to any person to drive delivery vehicles and be productive on day one."

Fixing Supply Chains One Mile At A Time

At a glance, it may be hard to connect the dots between a gargantuan freight ship stuck in the Suez Canal, say, and your overnight package being delayed

But there is, in fact, a continuity.

“When we think about ‘last mile’ problems, it could actually mean both first mile and last mile. First mile being the pickup of something, and then the last mile is the drop-off at a given location,” Mantri explains.

When complications arise in the “middle mile”—for example, in moving goods across borders—they trickle down. “Whether it’s having enough containers at ports or trucks to unload containers and move them around or even space for ships and containers, there can always be transportation issues,” Mantri says.

That’s why it’s so important to shorten that final leg of the journey as much as possible. By moving “more of the manufacturing, sourcing, assembly, transportation and inventory closer and closer to the last mile, you take a lot of those risks out of the equation,” Mantri says.

Finally, putting packages in customers’ hands must also be as efficient as possible. Often, it’s not a question of having enough trucks and drivers to deliver the day’s packages. For humans and algorithms alike, success depends on knowing what a fleet is doing at any given moment and understanding what impacts a driver’s ability to efficiently perform their deliveries.

Before the digital age, this information “lived inside drivers’ heads,” DeMeuse says. “Historically, if you look at fleet operations, your driver routes were kind of a black box. You didn’t know if they were going to follow your route. You didn’t know until after the fact if a package was delivered.”

Missed deliveries not only are a nuisance to consumers but also can have a significant monetary impact on delivery companies.

“If a delivery is not successful on its first attempt, that package or delivery as a whole can be unprofitable for our customers,” Mantri says. “It’s very important that they successfully deliver on the first attempt.”

Here, Google Maps Platform’s new Last Mile Fleet Solution can help fleet managers improve customer experiences and deliveries operations at scale. This solution allows companies to address every stage of the last-mile delivery journey: from address capture and route optimization to driver routing and navigation, shipment tracking and fleet performance insights.

“Without that visibility, it makes it really hard to improve things over time,” DeMeuse says. But “technology shifts are helping enable better visibility and predictability, and that’s what we’re trying to lean into with the Last Mile Fleet Solution.”

The Ongoing Project Of Mapping The World

Whether they’re moving freight around the world or delivering hamburgers across town, today’s mobility service providers have the unenviable task of picking up the pace, making no mistakes and keeping costs down.

That’s why more are coming to see the value of platforms that can provide geospatial intelligence and insights to help them differentiate their businesses.

The capabilities required to offer these insights don’t come easily, DeMeuse notes.

“It’s hard work because the world changes so dramatically,” he says. “That’s where Google is really invested. We will continue building technology to understand and map the world on an ongoing basis—and use that to enable developers through Google Maps Platform.”

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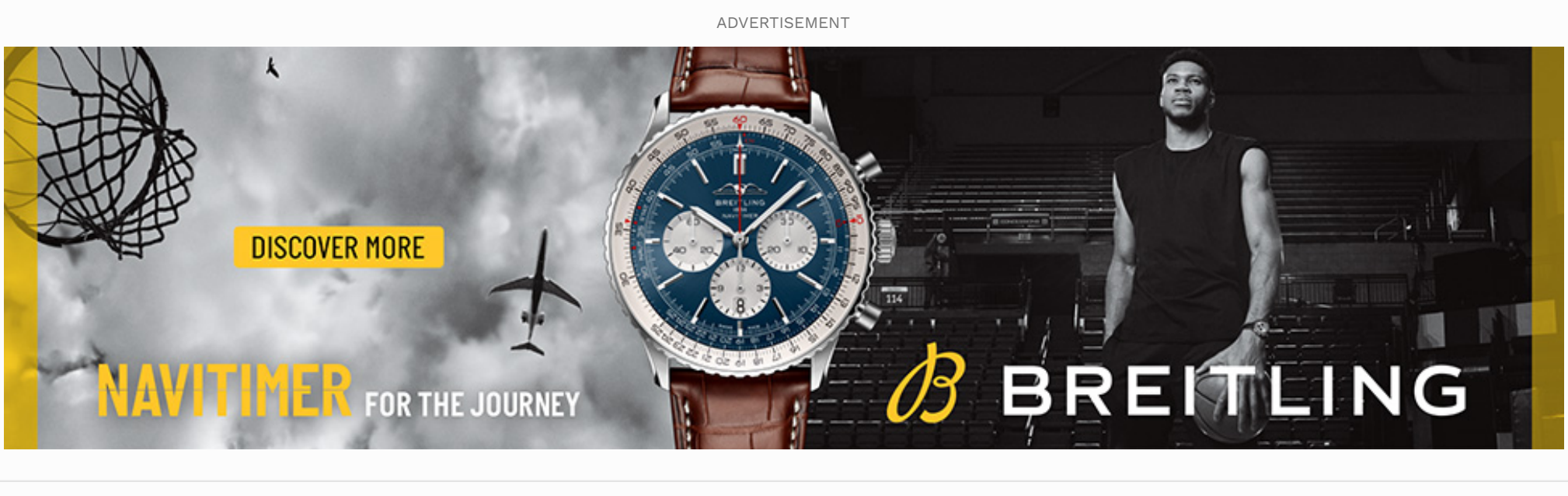

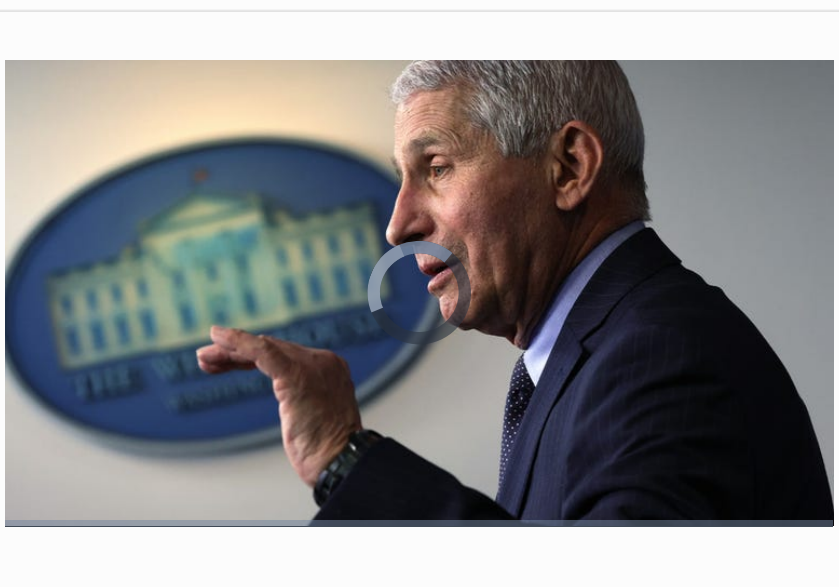

HEALTHCARE

SIDS Cause Is Not Known, Despite What New Study Claims

Nina Shapiro Contributor
Dispelling health myths, fads, exaggerations and misconceptions.

May 20, 2022, 09:45am EDT

Sleeping newborn GETTY

Sudden Infant Death Syndrome, or SIDS, is every new parent’s worst nightmare. SIDS is an unexplained death of a sleeping infant under the age of 12 months. It most commonly occurs between ages one and six months. While the cause remains unknown, there are multiple well-known risk factors for SIDS, as well as multiple well-known measures to minimize these risks.

A study published in the open access journal *eBioMedicine* in early May 2022 made headlines, as its results stated that a biochemical marker as the cause of SIDS was found. The study group, based in Australia, analyzed blood samples taken at birth of over 600 newborns. Those that died due to SIDS were found to have a relatively lower level of a substance known as BChE, or butylcholinesterase. Low levels of BChE have been explored as potential biomarkers for neurodegenerative conditions such as Alzheimer’s Disease. This substance acts in the part of the nervous system called the autonomic nervous system, which is responsible for bodily functions such as blood pressure regulation and respiratory rate and drive. The study’s findings suggest that if an infant’s BChE level is low at birth, this may be a marker for SIDS in the coming months.

Newborn blood test GETTY

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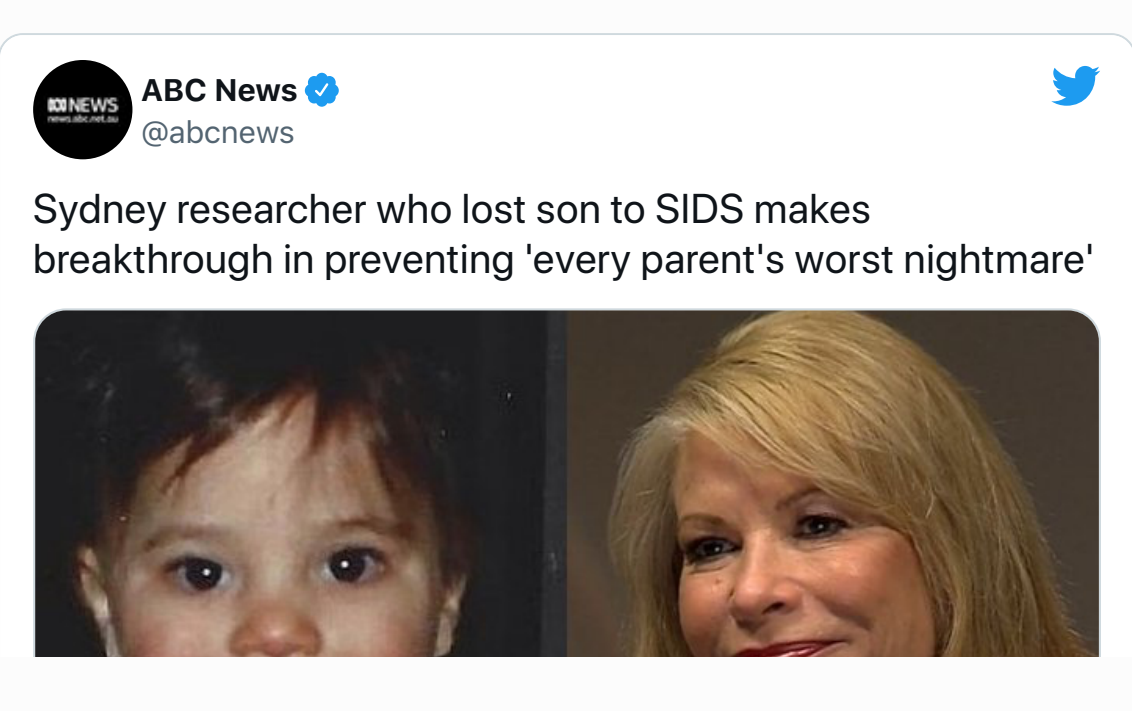
Within a few days, this story went viral, with many outlets lauding the researchers that they had finally found the cause for SIDS.



ABC News
@abcnews

Sydney researcher who lost son to SIDS makes breakthrough in preventing 'every parent's worst nightmare'

But then came the pause. As is the case with so much in science, if it sounds too good to be true, it probably is. While this finding may, indeed, be a marker to explore further, calling it the cause of SIDS is not only an exaggeration, it is also not the case. At least not to our knowledge. Yet.

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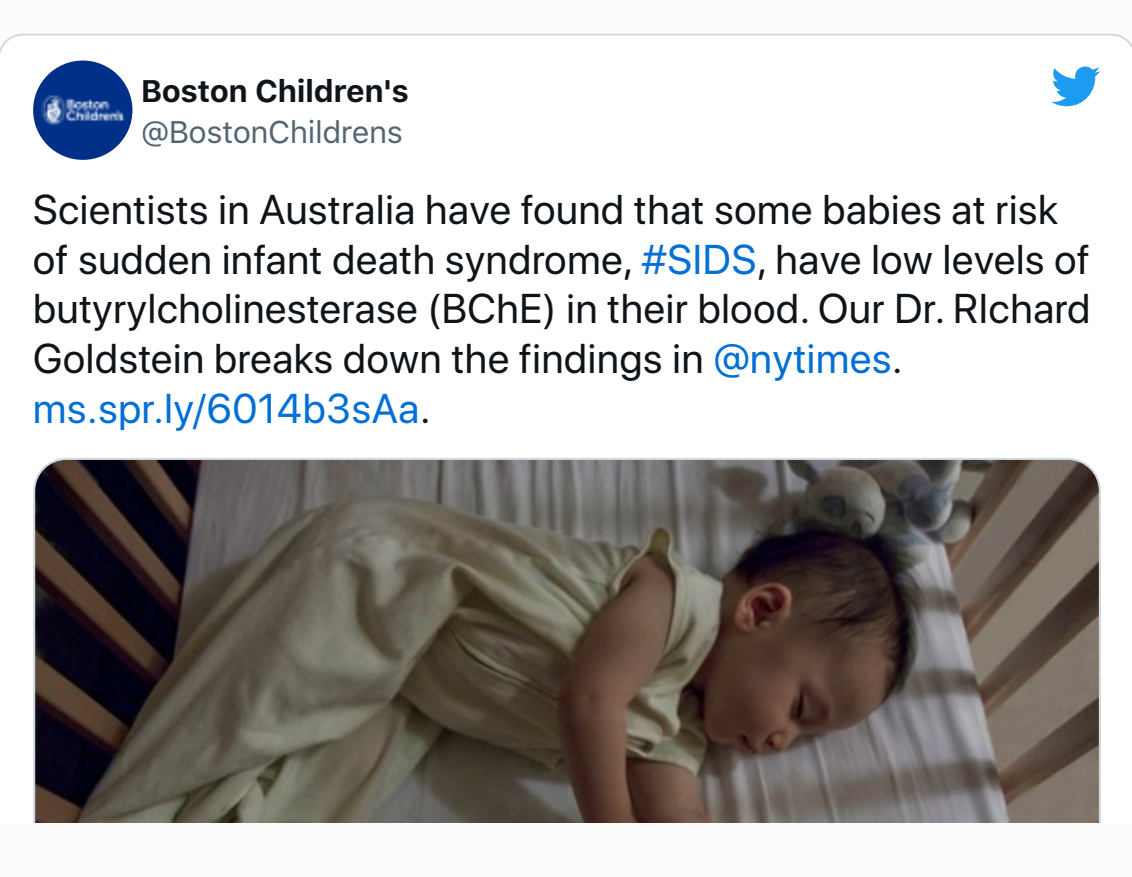
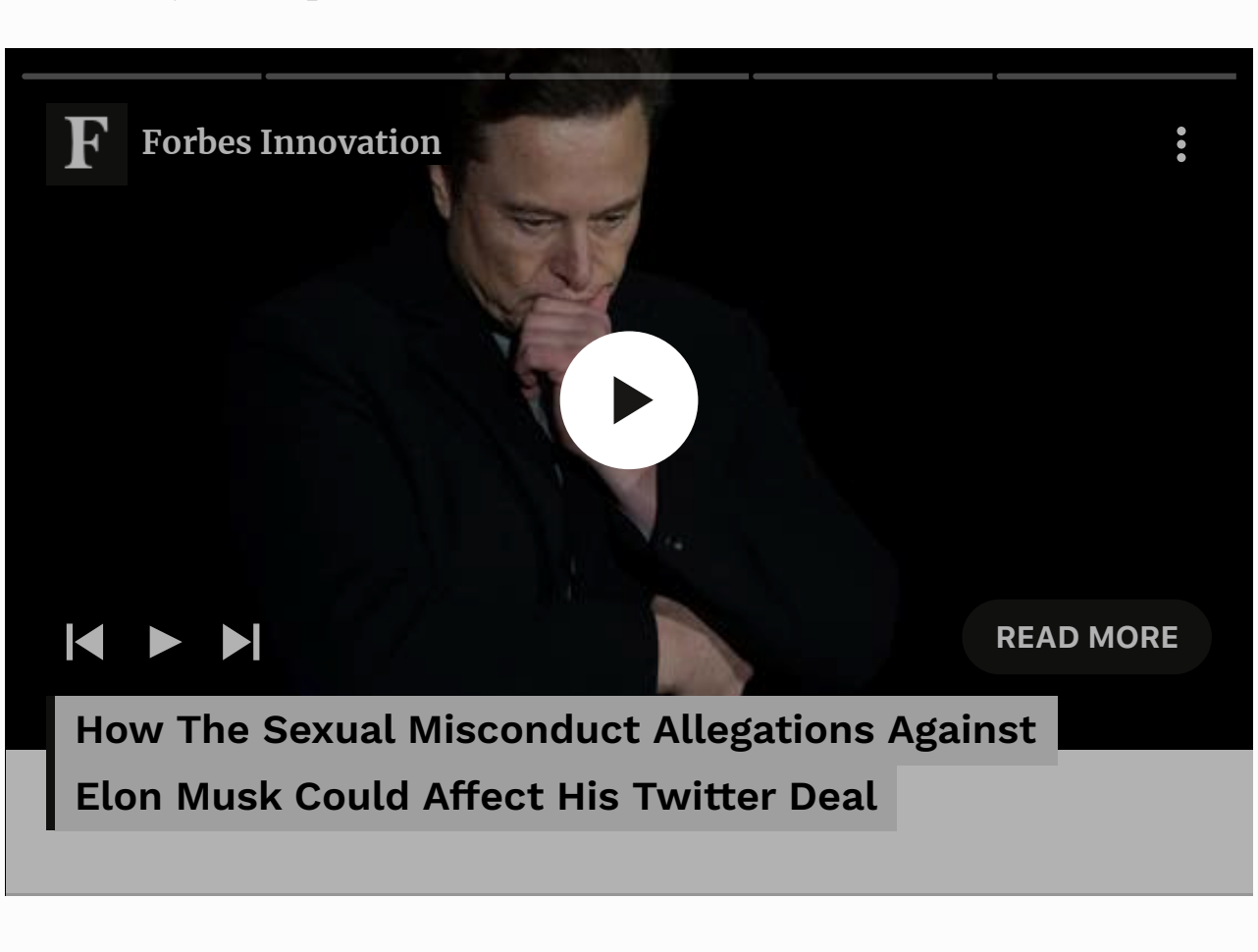


Boston Children's
@BostonChildrens

Scientists in Australia have found that some babies at risk of sudden infant death syndrome, #SIDS, have low levels of butyrylcholinesterase (BChE) in their blood. Our Dr. RIchard Goldstein breaks down the findings in @nytimes. ms.spr.ly/6014b3sAa.

As described by Dr. Benjamin Mazer in the May 17, 2022 issue of *The Atlantic*, the explosion of this small study’s findings skipped so many critical steps in the scientific process of learning about cause and effect of a fatal event. The study, which examined the blood of 600 babies, 26 of who died of SIDS, found *overall* lower levels of BChE than those who didn’t succumb. But this was a lower level on average, not a binary on or off switch of “all or none.” It’s not that the study was not a good one, but it is that it was not a definitive study of “cause and effect.” It was barely one of “association.” Some babies who did not die of SIDS had low levels of BChE. Some who did die had normal levels of BChE. Could there be an association between low levels of BChE and risk for SIDS? Certainly. But to call it the cause, based on this small study, is not possible.



How The Sexual Misconduct Allegations Against Elon Musk Could Affect His Twitter Deal

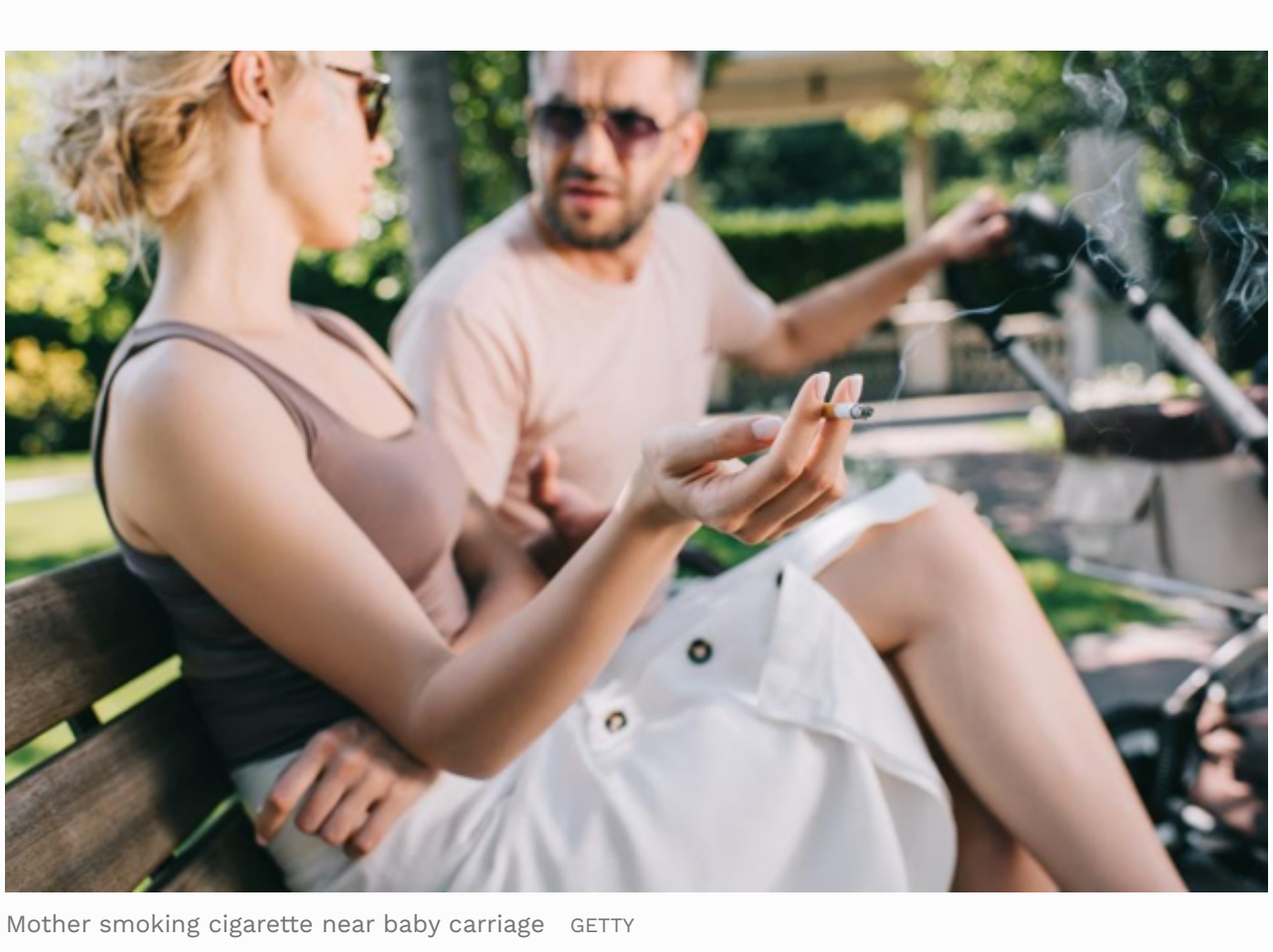
As Dr. Mazer points out, even if low BChE were found to be a notable biomarker for SIDS risk, we already know that there are multiple risk factors for SIDS, and many ways to lower these risks. Foregoing these mitigation measures would be dangerous.

Newborn on back GETTY

In the 1990’s, the American Academy of Pediatrics began the “Back to Sleep” campaign, urging parents and caregivers to place newborns on their backs when placing them to sleep. This position significantly lowers the risk of both suffocation if an infant’s nose and mouth are flat against a crib sheet, and also lowers the risk of an infant re-breathing their own carbon dioxide while facing down during sleep. This campaign increased awareness of this and other safe sleep practices, leading to a reduction in annual SIDS deaths in every subsequent year.

However, even with the benefits of safer sleep practices, SIDS remains a devastating event for several thousand infants annually in the United States alone. There are other known risk factors for SIDS besides stomach sleeping, such as history of premature birth, second-hand smoke exposure, use of a soft crib mattress or presence of blankets, pillows, or toys in a crib, and overheating a baby during sleep.

To reduce risk of SIDS, a baby should sleep on their back on a firm crib mattress with no blankets, no pillows, no crib bumpers and no toys. Room temperature should be comfortable yet not too warm. Higher room temperature (and summer months) tend to be associated with (but not the cause of) SIDS.



Mother smoking cigarette near baby carriage GETTY

Indeed, had there been one cause, or a few causes clearly being the source of the horror of SIDS, it would be absolute cause for celebration. Unfortunately, it’s just not the case. The findings are valid, and potentially an important piece of the very complex puzzle that is SIDS. But a tweet stating “They found the cause of SIDS”, which quickly went viral, is misleading at best, and harmful at worst.

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Nina Shapiro

I wrote a book dispelling health myths called HYPE: A Doctor's Guide to Medical Myths, Exaggerated Claims and Bad Advice-- How to Tell What's Real and What's… **Read More**

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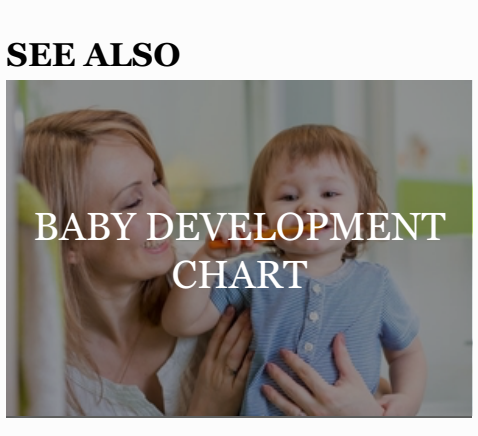

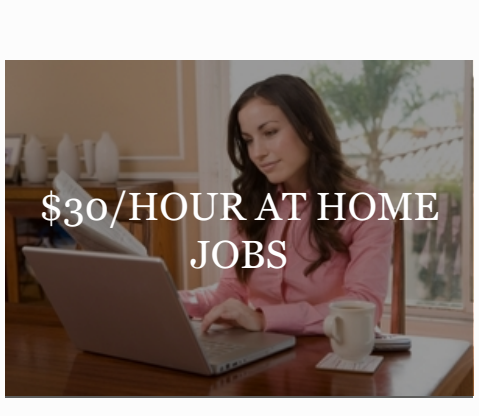

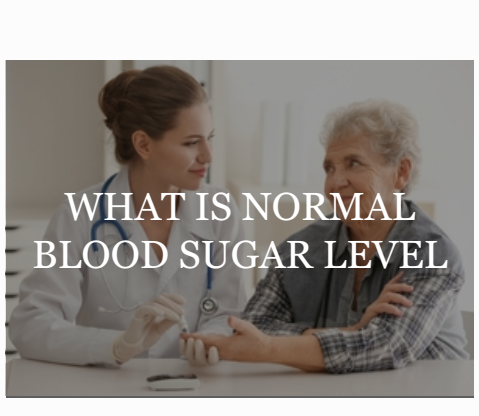
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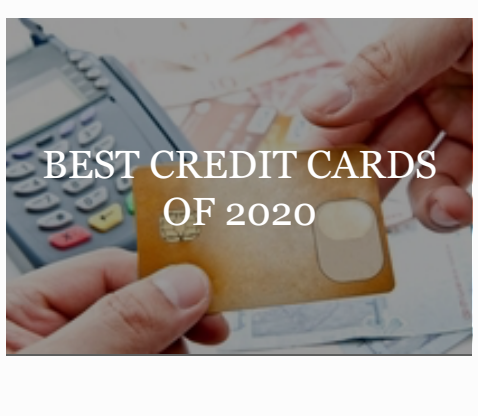

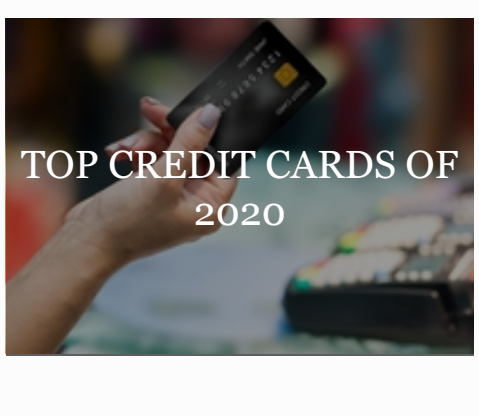

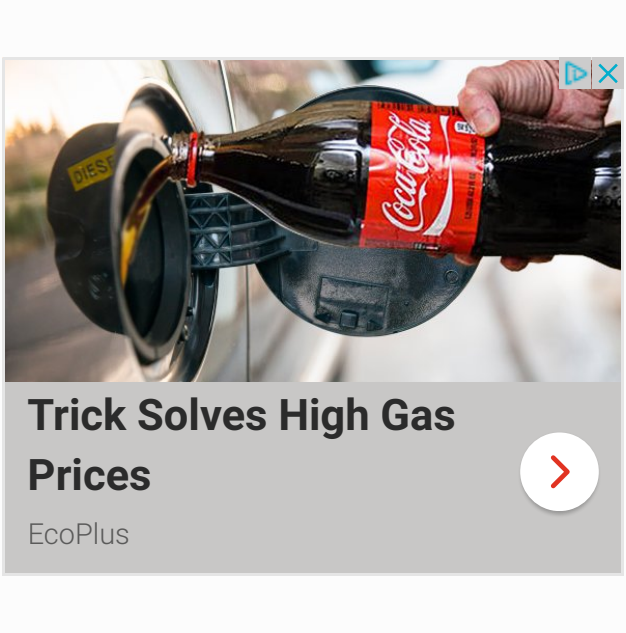
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HEALTHCARE

Paxlovid Rebound: FDA Investigating Reports Of Covid-19 Relapses After Taking Pfizer Antiviral

Bruce Y. Lee Senior Contributor
I am a writer, journalist, professor, systems modeler, computational and digital health expert, avocado-eater, and entrepreneur, not always in that order.

May 19, 2022, 09:30pm EDT

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There have been more and more stories of people suffering worsening of Covid-19 symptoms shortly ... [+] DPA/PICTURE ALLIANCE VIA GETTY IMAGES

Having a rebound of Covid-19 after taking Paxlovid is not exactly the same as having a rebound relationship. Although both could make you sick in different ways. A post-Paxlovid rebound may come after you feel better from taking Paxlovid for a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The rebound is when at some point after the five-day course of the medication is completed, you experience a relapse of Covid-19 symptoms. And it seems like more and more people have been reporting such relapses.

For example, there’s that pre-print case report uploaded to *Research Square* on April 26, 2022, of a 71-year-old man who had been fully vaccinated and boosted against Covid-19. He began taking Paxlovid as soon as he had tested positive for Covid-19, two days after he had gotten exposed to the virus. His Covid-19 symptoms essentially disappeared after two days of Paxlovid, which seemed like a good thing. Yet, nine days after he had first tested positive and four days after he had completed the five-day course of Paxlovid, guess what happened? His runny nose, sore throat, and difficulty breathing returned, along with SARS-CoV-2 levels in his body going up again. It was like déjà eww all over again. Viral genome sequencing showed that during both his initial symptoms and his return of symptoms, he was infected with the BA.1 Omicron subvariant of the SARS-CoV-2. This suggested that he has experienced not two separate infections but a single one that improved before subsequently getting worse.

Of course, a pre-print is not the same as a peer-reviewed article, and anyone with opposable thumbs, a laptop, and Internet access could in theory upload a pre-print. But the authors of the case report (Kalpana Gupta, MD, Judith Strymish, MD, Gary Stack, MD, PhD, and Michael Charness, MD) are legitimate doctors from legitimate healthcare systems, the VA Connecticut and Boston Healthcare Systems. Plus this certainly hasn’t been the only report of such a rebound. For example, here’s what Tatiana Prowell, MD, an Associate Professor of Oncology at the Johns Hopkins School of Medicine, tweeted:

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And Peter Hotez, MD, PhD, Dean of the National School of Tropical Medicine at Baylor Medical College, described his case of possible post-Paxlovid relapse in the following tweet:

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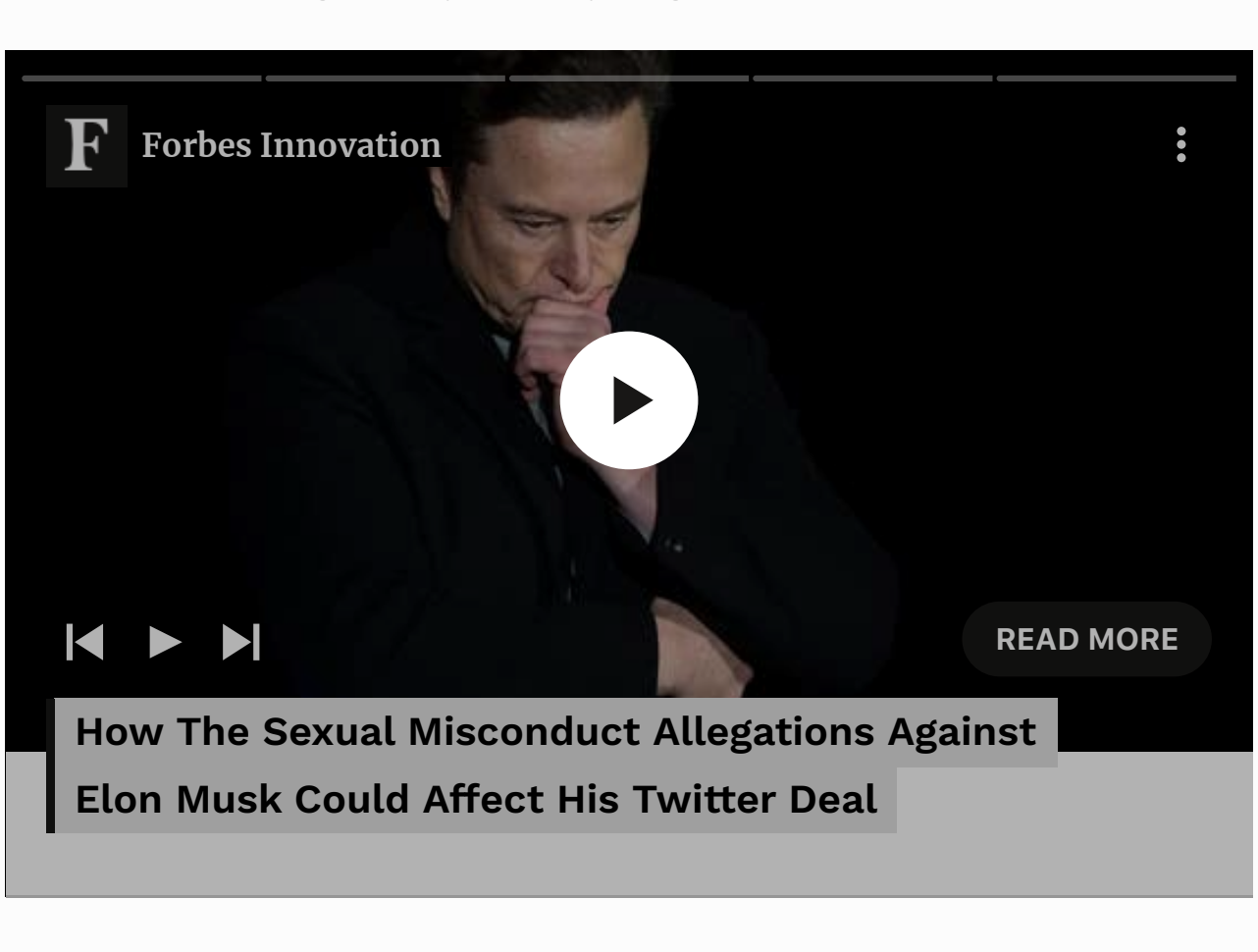
As a reminder, Paxlovid received an emergency use authorization (EUA) back on December 22, 2021, from the U.S. Food and Drug Administration (FDA) as a treatment for those 12 years and older with mild-to-moderate Covid-19. These antivirals are supposed to keep the SARS-CoV-2 from doing the nasty in your body, which is a non-technical way of saying reproducing in your cells. While Paxlovid doesn’t amount to putting tiny little condoms on the viruses’ spikes, it is actually the combination of two different antiviral tablet, nirmatrelvir and ritonavir, packaged together like Hall & Oates. The recommended dose of these antivirals is two 150 mg tablets of nirmatrelvir along with one 100 mg tablet of ritonavir twice a day for five days, assuming that you have normal kidney function.

Like peanut butter and jelly, these two medications are supposed to work together. Nirmatrelvir can block the action of an enzyme called M^{PRO}, not to be confused with GoPro. M^{PRO} cleaves two different viral polyproteins, which may not sound very sexy but is an important step when the SARS-CoV-2 wants to reproduce. Meanwhile, ritonavir can inhibit cytochrome P450 (CYP) 3A4 enzymes in the liver that can break down nirmatrelvir, thus allows nirmatrelvir to hang out in your body longer.



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And just like condoms, Paxlovid doesn’t work *after* reproduction has already occurred. That’s why it’s important to take Paxlovid as soon as you’ve learned that you are positive for Covid-19. Waiting beyond five days after symptoms first appeared may allow the virus to reproduce too much for Paxlovid to make much of a difference. So there is a finite window, less than half a Scaramucci, during which taking Paxlovid will help.

But what then about these reported rebound cases, where people seemed to do what they were supposed to do and take the medication as soon as they were diagnosed with Covid-19? As this *NBC News* segment shows, the FDA is currently investigating the reports of Covid-19 rebound cases:

Do these rebound cases then mean that Paxlovid is not doing its job? No, not necessarily. Just because symptoms return doesn't mean that things wouldn't have been even worse without the medication. Plus, it's not yet clear what percentage of people have been experiencing such relapses. Again, stories on Twitter and a pre-print case report ain't the same as peer-reviewed studies. While Pfizer's clinical trial did show possible rebound Covid-19 occurring in about 2% of those who had received Paxlovid, around 1.5% of those who had received only placebo also suffered similar relapses. With these two percentages not being statistically significantly different from each other, the conclusion from the clinical trial was that these rebounds weren't specific to Paxlovid. Of course, what happens or doesn't happen in a clinical trial doesn't necessarily mean the same will apply exactly in the real world.

So what's going on, in the words of Marvin Gaye? One possibility is that the five-day course of the medication is turning out to be not long enough for everyone. The medication is supposed to suppress viral replication long enough for your immune system to clear the virus from your body. It's kind of like smearing deodorant on yourself until you've had a chance to take a real shower. Remember Paxlovid doesn't clear the virus from your body. It just keeps it from replicating. The amount of time needed for your immune system to accomplish this virus-clearing task may vary depending on how much virus happens to be in your body and the status of your immune system. It could be that your immune system hasn't geared up enough before the five-day course of the medication has been completed. So one question is whether the course of Paxlovid should be longer than five days.

Another possibility is that the Omicron variant may be different enough from previous versions of the virus that the medication may not be quite as effective. Remember Pfizer's clinical trial occurred last year while the Delta variant was dominant. So all results from the clinical trial may be more Delta-specific.

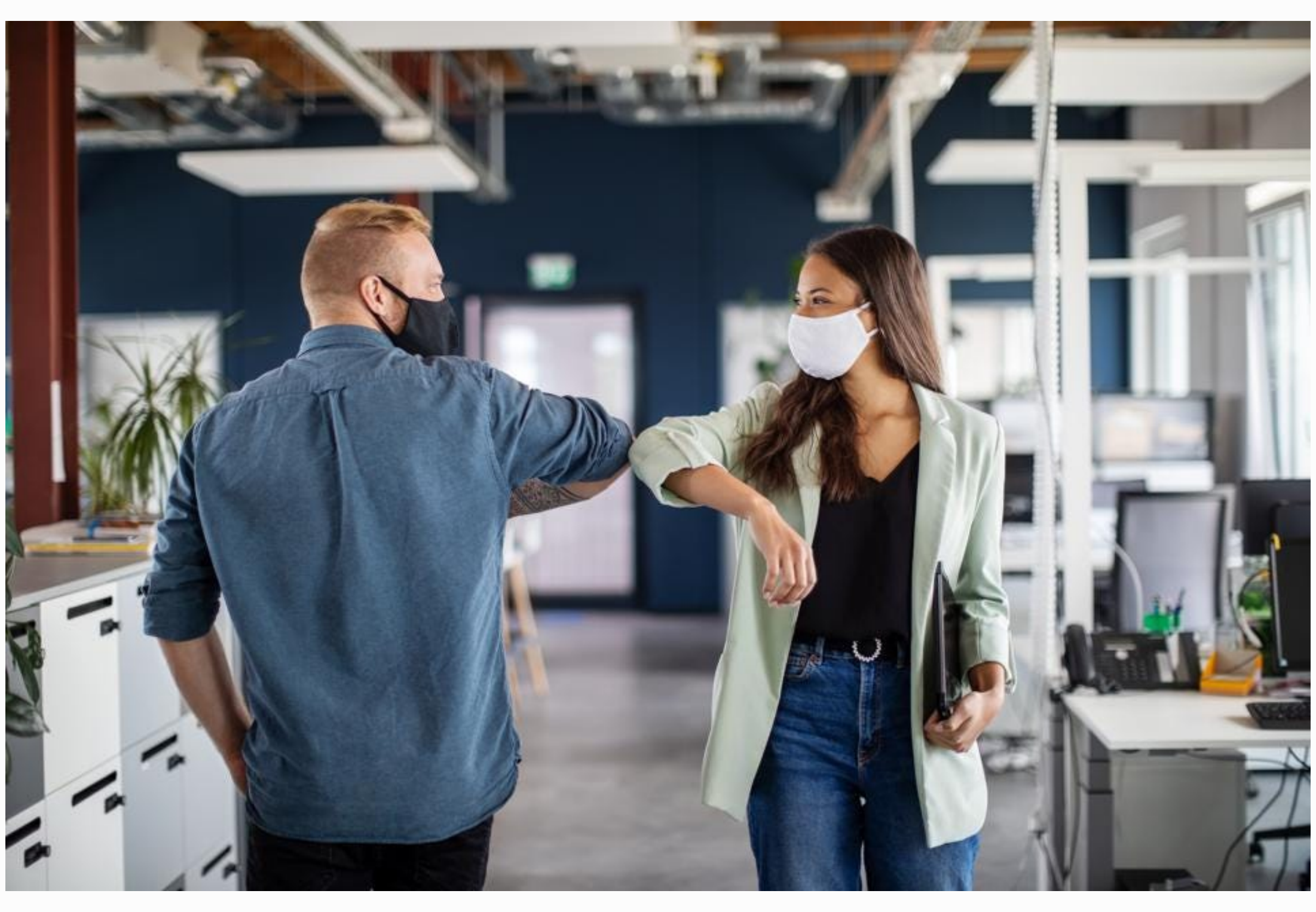
A third possibility is that the virus has been developing resistance to the antiviral medication. While resistance may not be futile, it can reduce the effectiveness of the medication. Resistance is why flu antivirals such as Tamiflu may not be as effective against certain strains of the flu. And with the Covid-19 coronavirus replicating so much, resistance could very well develop. After all, each time the SARS-CoV-2 replicates, it can be like a drunk person making photocopies of his or her butt using the office photocopying machine. Mistakes can result when the virus tries to copy its genetic code leaving resulting progeny with mutations and thus different genetic sequences. Some of these mutations may alter virus proteins enough to allow the virus to better evade the antiviral.

Many people using the antiviral medication could then end up selecting for viruses with such resistance mutations, because such resistant viruses would be better able to survive. These resistant versions could then eventually become the dominant version of the virus. That's why antiviral medications shouldn't be overused.

While there was no clear evidence of resistance developing during the Pfizer Paxlovid clinical trial, the trial may not have gone on long enough to see this possibility. It will be important for public health officials to track the possible emergence of resistant virus strains and potentially limit the use of Paxlovid if such resistance were to be found.

A fourth possibility is re-infection. Could some of the supposed relapse cases actually be people getting infected and then re-infected in a short period of time? I did cover for *Forbes* a case of someone getting infected with the Omicron variant within 20 days of first getting infected with the Delta variant. But it's not clear how common such getting two separate infections within such a short time period may be.

So if you do have a rebound case of Covid-19 after taking Paxlovid, what should you do? Should you take more of this antiviral medication? Well, currently, things are about as clear as Nutella soup. There is not enough evidence about what to do. And the EUA only covers taking the medication for a single five day course.



As long as the Covid-19 pandemic is still going on and the virus is circulating widely around you, ... [+]
GETTY

Ultimately, more studies, more data, and more drug surveillance are needed. All of this is a reminder that while Paxlovid may be a very useful part of dealing with the pandemic, it is not a magical pill. Nothing in life is a magical solution with the possible exception of avocados or chocolate. Relying solely on a medication to "rescue you" if you were to get Covid-19 could be like relying on finding a soul mate to rescue you from your current life.

Don't think that the existence of Covid-19 treatments can allow you to forego other Covid-19 precautions such as face mask wearing and vaccination against Covid-19. Remember Covid-19 interventions are like Swiss cheese, not that you should start putting them on your ham sandwich. Rather, this means that each individual precaution or treatment has its specific set of holes. And the hole thing means that you should always be layering at least several Covid-19 precautions on top of each other as long as the pandemic is still going on and the virus is circulating widely around you. If you don't maintain other Covid-19 precautions and rely solely on getting Paxlovid when needed, the Covid-19 coronavirus could very well catch you and potentially catch you on the rebound, too.

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Bruce Y. Lee

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